REMARKS

Responsive to the action mailed March 7, 2002, Applicants provisionally elect the invention of Group I. The election is made with traverse.

Applicants respectfully request modification of the restriction requirement. In particular, Applicants submit that the restriction of claims 17-22 into five groups and claims 23-27 into five groups is improper. These claims do not present a serious search burden, because each recited inhibitor relates to IL-1β and a search for inhibitors is likely to uncover the relevant prior art.

Applicants have amended claims 1-5, 7-10, and 15 for grammatical clarity and to adjust claim dependencies. Claim 6 has been canceled. In addition, claim 3 has been amended to recite a method for diagnosing multiple myeloma in an individual. Support for this amendment can be found throughout the specification (e.g., at page 3, lines 26-29, page 8, lines 15-23, and page 9, lines 7-10). Claim 15 has been amended to recite a method of monitoring the status of multiple myeloma in an individual. Support for this amendment is found in the specification at, for example, page 5, lines 1-5, and page 10, lines 4-12.

New claim 28 depends from claim 1, and recites that the bone marrow preparation is from an individual diagnosed with a multiple myeloma-related plasmaproliferative disorder. Support for this new claim is found throughout the specification.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants believe that no additional fees are due. If this is incorrect, please apply any charges to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the specification:

Paragraph beginning at page 1, line 3 has been amended as follows:

This invention was made with Government support from the National Institutes of Health, grant number CA62242. The Government has certain rights in the invention.

In the claims:

Claim 6 has been cancelled.

Claims 1-5, 7-10, and 15 have been amended as follows:

1. (Amended) A method of quantitating IL-1β in a bone marrow preparation comprising: [;]

a) [culturing stromal cells with said bone marrow prep aration;

b)] determining the amount of IL-6 produced by [said] stromal cells cultured with said bone marrow preparation; and

b [c]) correlating the amount of IL-6 produced by said stromal cells to the amount of IL-1β [concentration] in said bone marrow preparation [by comparison to a standard curve prepared by measuring IL-6 produced by stromal cells contacted with known concentrations of IL-1β].

2. (Amended) The method of claim 1, wherein said bone marrow preparation is from an individual diagnosed with [a patient suffering from] multiple myeloma [(MM) or a multiple myeloma-related plasmaproliferative disorder].

3. (Amended) A method of diagnosing [detecting] multiple myeloma [(MM)] in an individual, said method comprising[:

a) culturing stromal cells with a bone marrow preparation from said individual; and

b)] determining the amount of IL-6 produced by [said] stromal cells cultured with a

bone marrow preparation from said individual, wherein an elevated level of IL-6 is indicative of multiple myeloma [MM].

4. (Amended) A method of determining likelihood of progression [identifying a patient with a multiple myeloma-related plasmaproliferative disorder likely to progress] to active multiple myeloma in an individual, said method [(MM)] comprising[:

a) culturing stromal cells with a bone marrow preparation from said patient; and

b)] determining the amount of IL-6 produced by [said] stromal cells cultured with a bone marrow from said individual, wherein an elevated level of IL-6 indicates said individual is likely to [indicative of a likelihood said patient will] progress to active multiple myeloma [MM].

5. (Amended) The method of claim 5, wherein said individual has been diagnosed with a multiple myeloma-related plasmaproliferative disorder [is monoclonal gammopathy of undetermined significance (MGUS)].

6. (To be cancelled) The method of claim 4, wherein said multiple myeloma-related plasmaproliferative disorder is smoldering multiple myeloma (SMM).

7. (Amended) The method of claim[s] 4 [3] or 5 [4], wherein an elevated level of IL-6 is a concentration of IL-6 greater than the concentration of IL-6 [that] produced by stromal cells incubated with 1 pg/ml of recombinant IL-1β.

8. (Amended) The method of any one of claims 1-8 [7], wherein said bone marrow preparation is selected from the group consisting of a fresh supernatant from cultured bone marrow cells, a previously frozen supernatant from cultured bone marrow cells and a mononuclear cell preparation purified from bone marrow.

9. (Amended) The method of any one of claims 1-8 [7], wherein an inhibitor of IL-1β is added to said [the] stromal cells cultured with said bone marrow preparation [of step a)].

10. (Amended) The method of claim 10 [9], wherein said inhibitor of IL-1β is selected from the group consisting of an anti-ILβ antibody, a soluble IL-1 receptor [(sIL-1R)] type I, a

soluble IL-1 receptor [sIL-1R] type II, an IL-1 [interleukin-1] receptor antagonist, [(IL-1ra)] and an IL-1 TRAP.

15. (Amended) A method of monitoring the status [effectiveness of the treatment of a patient] of multiple myeloma in an individual, said method [(MM)] comprising:

a) [culturing stromal cells with a bone marrow preparation from said patient after the initiation of treatment;

b)] determining the amount of IL-6 produced by [said] stromal cells cultured with a bone marrow preparation from said individual, said individual diagnosed with and undergoing treatment for multiple myeloma, said bone marrow preparation obtained after initiation of said treatment; and

b [c]) comparing said amount of IL-6 with a known standard or a patient determined standard.

PENDING CLAIMS AS OF APRIL 8, 2002

1. A transgenic mouse comprising, in its genome, an expression construct comprising a nucleic acid encoding an oncogene operably linked to an inducible promoter, said transgenic mouse further comprising a genetic mutation that causes said transgenic mouse to have greater susceptibility to cancer than a comparable mouse not comprising said genetic mutation, wherein inducing said inducible promoter results in expression of said oncogene and formation of cancer in said transgenic mouse.

2. The transgenic mouse of claim 1, wherein not inducing said inducible promoter after said formation of cancer results in reduced cancer in said transgenic mouse.

3. The transgenic mouse of claim 1, wherein said oncogene is ras.

4. The transgenic mouse of claim 3, wherein said ras has an activating mutation.

5. The transgenic mouse of claim 1, wherein said inducible promoter is inducible by doxycycline.

6. The transgenic mouse of claim 1, wherein said genetic mutation is in DNA encoding a tumor suppressor.

7. The transgenic mouse of claim 6, wherein said tumor suppressor is INK4.

8. A transgenic mouse comprising, in its genome: (i) a first expression construct comprising a reverse tetracycline transactivator operably linked to a tissue-specific promoter; and (ii) a second expression construct comprising a nucleic acid encoding an oncogene operably linked to a promoter that can be regulated by said reverse tetracycline transactivator and doxycycline, said transgenic mouse further comprising a genetic